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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,986	11/21/2003	Mang Yu	NB-00101.P.1-US	3664

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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/718,986	YU ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-20,22-24,31-34,47, 50 , 54-58 and 61-73* is/are pending in the application.

4a) Of the above claim(s) *50 and 54-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,16-20,22-24,31-34,47 and 61-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. ***Election***

Applicant's election of Group I (claims 1-14, 16-20, 22-24, 31-34, 47 & 61-73) in reply filed 11/22/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. **Claims withdrawn** :

Claims 50 & 54-58, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Claims 1-14, 16-20, 22-24, 31-34, 47 & 61-73 are under consideration in this Office Action.

4. ***Priority***

Applicant's claim for domestic priority under 35 U.S.C. 119(e), filed 4/19/2003 & 11/22/2002, is acknowledged.

5. ***Drawings***

Drawings filed 11/21/2003 is acknowledged.

6. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

7. ***Written Description***

Claims 1-14, 16-20, 22-24, 31-34, 47 & 61-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. These claims are directed to a genus of protein-based compositions comprising a compound (fusion protein) that comprises: at least one [1]therapeutic domain having extracellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell; and pharmaceutical compositions thereof (claim 1). Dependent claims 2-14, 16-20, 22-24, 31-34, 47 & 61-73 identify target cell to be epithelial or endothelial, anchoring and therapeutic domains by the peptide names or sequence identifier number of one or the other domains, but lack the complete structure of the compound in any single claim nor specify having a defined function with respect to a specific pathogen or in preventing any specific infection.

The specification generally describes the compound to be one of the following (*see* pages 17 & 20):

1. (Anchoring domain)n-linker-(Protease Inhibitor)n (n=1,2,3 or more); or

2. (Protease Inhibitor)n-linker-(Anchoring domain) n (n=1,2,3 or more);

3. (Anchoring domain)n-linker-(Enzymatic activity)n (n=1,2,3 or more);

4. (Enzymatic activity)n-linker-(Anchoring domain)n (n=1,2,3 or more); does not contain any disclosure or description of the structure and function of all permutations and combinations of the compounds or its effectiveness in preventing any pathogenic infection.

The genus of compounds comprised by the compositions is a large variable genus which remain undescribed. Such a genus may also include many functionally unrelated compounds with no use in preventing any pathogenic infection. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. ***Enablement Rejection***

Claims 1-14, 16-20, 22-24, 31-34, 47 & 61-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for composition comprising specific fusion constructs comprising the specific domains including structure and the associated function, that may be obtained by substituting these domains in the following equations:

1. (Anchoring domain)n-linker-(Protease Inhibitor)n (n=1,2,3 or more); or

2. (Protease Inhibitor)n-linker-(Anchoring domain) n (n=1,2,3 or more);

3. (Anchoring domain)n-linker-(Enzymatic activity)n (n=1,2,3 or more);

4. (Enzymatic activity)n-linker-(Anchoring domain)n (n=1,2,3 or more); (if it can be measured) sequence of SEQ ID NO: 3,

does not reasonably provide enablement for any composition comprising compounds of undetermined structure and function be used for preventing pathogenic infection.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of compounds (fusion protein constructs) broadly encompassed by the claims.

The nature of the invention and the breadth of the claims: The claimed invention is drawn to a These claims are directed to a protein-based compositions comprising a compound (fusion protein) that comprises: at least one [1]therapeutic domain having extracellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell; and pharmaceutical compositions thereof (claim 1). Dependent claims 2-14, 16-20, 22-24, 31-34, 47 & 61-73 identify target cell to be epithelial or endothelial, anchoring and therapeutic domains by the peptide names or sequence identifier number of one or the other domains, but lack the complete structure of the compound in any single claim nor specify having a defined function with respect to a specific pathogen or in preventing any specific infection. The instant claims encompass *in vivo* therapy as evidenced by the claims to a pharmaceutical composition. The claims are also drawn to variants and fragments of the 2 domains included in the fusion protein.

The state of the prior art and the level of predictability in the art:

The art teaches that the efficacy of the therapeutics is dependent upon factors such as solubility of the drug,

bioavailability at the target site, attainment of effective plasma concentration, solubility in tissues, biotransformation, toxicity, proteolytic degradation, immunological inactivation, rate of excretion or clearance (half-life), deactivation by the liver, hydrolysis in serum, and binding to plasma protein, see Benet et al., pp. 3-32, in Pharmacological Basis of Therapeutics, 8th ed., 1990, page 3, first paragraph; page 5, second column, last partial paragraph, first two sentences; page 10, the paragraph bridging columns 1 and 2; page 18, the paragraph bridging columns 1 and 2; page 20, last full paragraph; and the paragraph bridging pages 20 and 21.

The amount of direction provided and the existence of working examples: Given "the teachings of unpredictability regarding the efficacy of fusion molecules for in vivo therapy, detailed teachings are required to be present in the specification sufficient to overcome the teachings of unpredictability which are found in the art. Such teachings are absent. While the specification makes the general statement that the fusion proteins of the claimed invention are useful for preventing infection in a target cell in vitro and in vivo, there is no guidance as to how to accomplish this in vivo. There appears to not even one clear working example of preventing infection in a target cell with a fusion protein.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support Applicants' claim to functional

pro-apoptosis-modifying fusion proteins capable of binding a target cell in vivo. All of the factors considered in the sections above, underscores the criticality of providing working examples in the specification for an unpredictable art such as preventing infection in a target cell with a fusion protein in vivo.

Quantity of experimentation needed to make or use the invention based on the content of the disclosure: In view of the Wands factors considered above, one of ordinary skill in the art would conclude that preventing infection in a target cell using a fusion protein in vivo would require undue experimentation in order to use the invention as claimed by the Applicants.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the compound (fusion protein) that comprises: at least one [1]therapeutic domain having extracellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. ***Pharmaceutical composition***

Claims 47 & 72-73 rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited

to a composition of specific fusion protein construct(??) as indicated in paragraph 8 above.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988) [*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

It is neither taught nor any data is provided for using the specific fusion protein construct in pharmaceutical compositions for the treatment and or prevention of any of the diseases or disorders or infections. There is no evidence presented that specific fusion protein construct(??) is associated with any of the known diseases or disorders or infections or can be treated or prevented by administering the specific fusion protein construct(??). Without such a data or evidence, claims to pharmaceutical composition comprising specific fusion protein construct(??), would amount to a composition or potential drug for treatment for any disorder or disease or infection, which is not enabled. Given the lack of direction or guidance and the nature of the invention, obtaining such a composition for one of skill in the art would be highly unpredictable. This is because the specific fusion protein construct(??) when associated with a particular disease or disorder or infection would be expressed differentially. Manipulating or controlling these levels depends upon the disease or disorder or infection, and may not always be

controlled by supplementing with such a specific fusion protein construct(??) composition. Further, no guidance in provided, pertaining to the fate of the administrated specific fusion protein construct(??) *in vivo*.

Since it is not routine in the art to engage in *de novo* experimentation to prepare numerous compositions where the expectation "of success is unpredictable", the skilled artisan would require additional guidance, specific to individual disorder or disease or infection, in order to make and use pharmaceutical compositions in a manner reasonably commensurate with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

10. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 63 & 70-71 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 63, recites 'wherein the at least one bacterial sialidase is one bacterial sialidase'. This does not read right, grammatically. It is not clear what the Applicants intend to claim.

Claim 70, recites 'wherein the at least one anchoring domain is at least two anchoring domain.' As in claim 63, it is not clear what the Applicants intend to claim.

Suitable corrections are required to overcome this rejection.

Claim 71 is included in the rejection for failing to correct the defect present in the base claim(s).

11. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-4, 47, 65, 70 are rejected under 35 U.S.C. 102(e) as being anticipated by Youle et al. (USP 6,737,511, 8/16/1999).

The instant claims are broadly drawn to a protein-based composition comprising a compound (fusion protein) that comprises: at least one [1]therapeutic domain having extracellular activity which may be catalytic or inhibitory and that can prevent infection of target cell; and one [2]anchoring domain which may be a binding domain (*see* specification pages 12-14 for the instantly stated definitions) and that can bind at or near the surface of the target cell; and pharmaceutical compositions thereof.

Youle et al. teach apoptosis-inhibiting fusion protein composition comprising: (1) first domain or an inhibitory domain, (2) a second domain capable of targeting the fusion protein to the target cell which is the similar in function as the anchoring or binding domain of the claimed construct and (3) a linker connecting the first and the second domains (see claims 1-12,

abstract, examples, and the entire patent). All claim limitations being taught the reference is anticipatory.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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